



Quest for a Global Influenza Vaccine Solution

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Novavax, Inc*

*International Vaccine Technology Workshop
Hyderabad, India
18 September, 2010*



Attributes of a Global Vaccine Solution

- ❑ Safe and immunogenic vaccine
- ❑ Rapid-response manufacturing technology



Mexico H1N1 Study

- ❑ Scaleability (Surge capacity)
- ❑ Economics



Rockville Plant

- ❑ Global Accessibility for in-border manufacturing
 - ❑ Cost and time to set up indigenous manufacturing
 - ❑ Ability to transfer technology

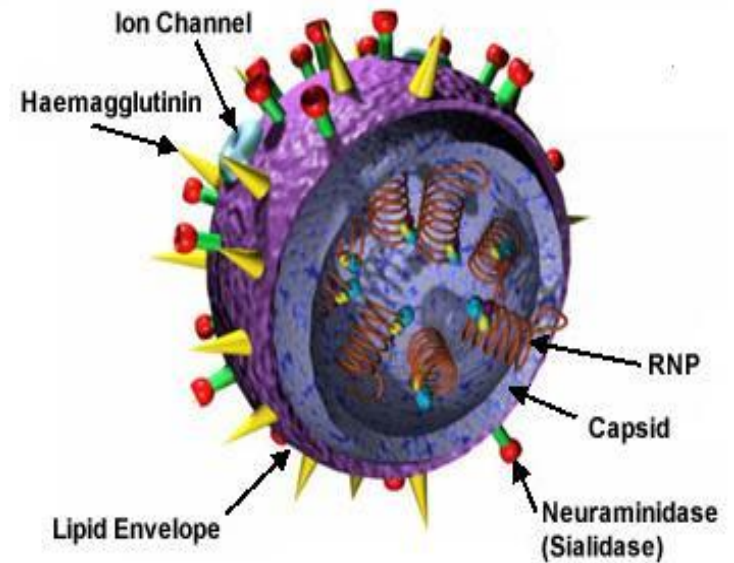


Cadila JV (India)
CPL Biologicals



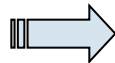
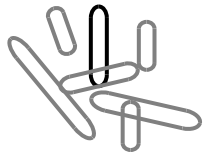
Recombinant Virus like Particle (VLP) Technology

- Select proteins important for inducing neutralizing antibody and CMI
 - Surface hemagglutinin (HA)
 - Neuraminidase (NA)
 - Matrix (M1)



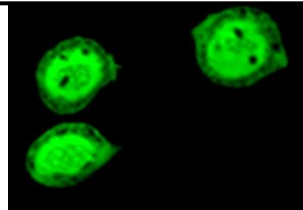
Genes coding for the HA, NA, and M proteins are put into baculovirus

rBaculovirus

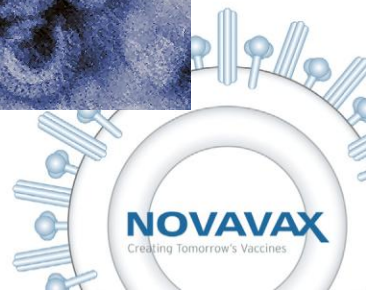
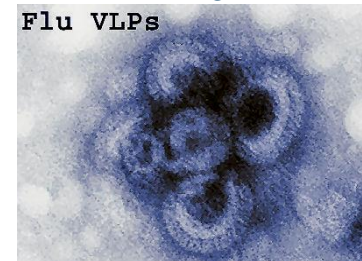


Infect cell culture (Sf9) with baculovirus

Baculovirus-infected Sf9 Cells



Proteins (HA, NA, M1) spontaneously form VLPs



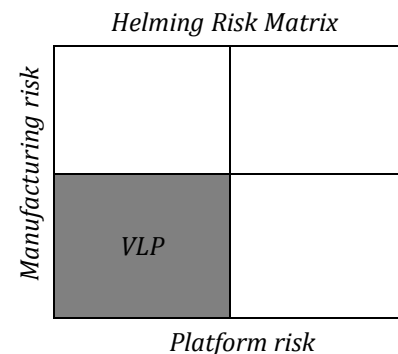
VLP is a Proven Vaccine Technology

VLP vaccines approved by U.S. Food and Drug Administration

- Hepatitis B vaccines (recombinant)
 - Recombivax[®] HB (Merck)
 - Engerix[®] B (GSK)
 - Multiple others
- Human papillomavirus vaccines (recombinant)
 - Gardasil[®] (Merck)
 - Cervarix[®] (GSK)

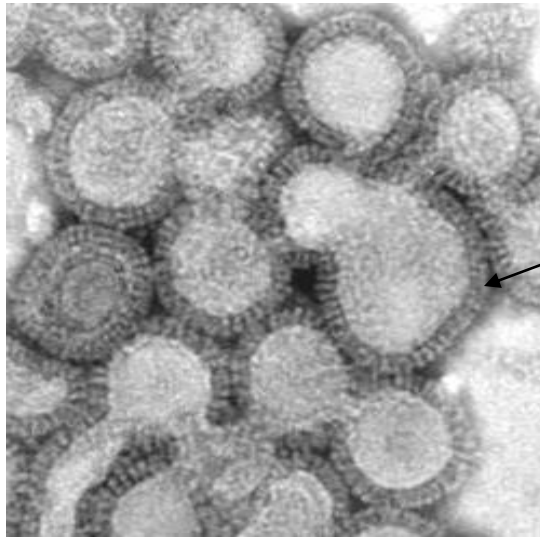
FDA approved vaccines produced using insect cells and baculovirus expression

- Cervarix[®] (GSK)
- Provenge[®] (Dendreon)



Potential Immunological Advantages of VLPs

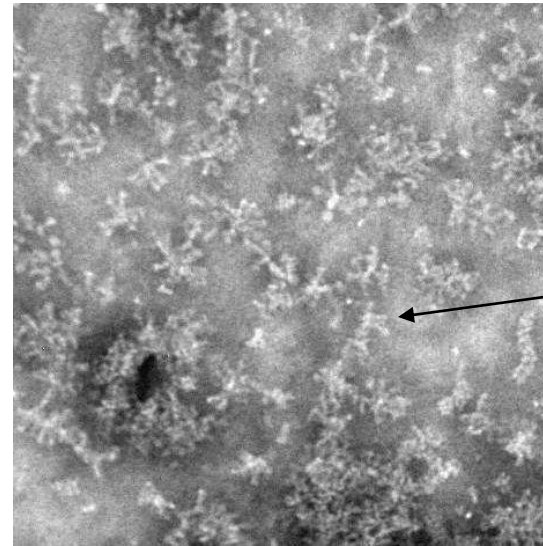
Novavax VLPs



HA and NA
spikes on lipid-
based
nanoparticles
(VLPs)

100nm

Fluzone 2008-09



HA subunits
Low or no NA

100nm

- HA – neutralizing Ab prevents infection
- NA – neutralizing Ab prevents virus release and cell spread
- HA and NA – No changes from egg or mammalian cell culture adaptation increasing genetic match
- VLPs – Potential for improved immune responses and broader protection



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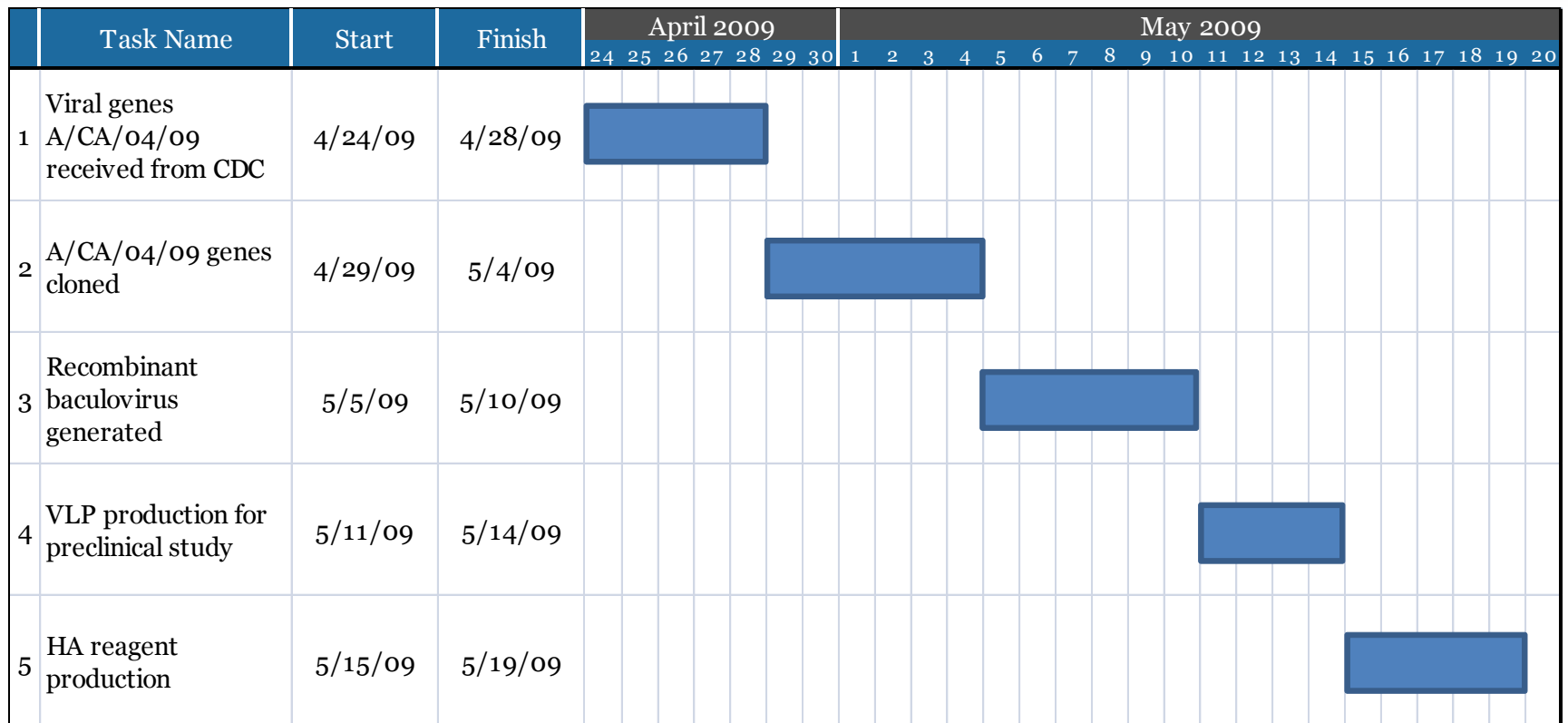


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VLP Technology Responds Fast

(2009 Pandemic H1N1 - Case Study)



- VLP vaccines can be produced in a fraction of the time of competing technologies
 - GLP batch produced in 4 weeks for ferret study
 - cGMP batch produced in 11 weeks
(vs. 4-5 months for competing technologies)

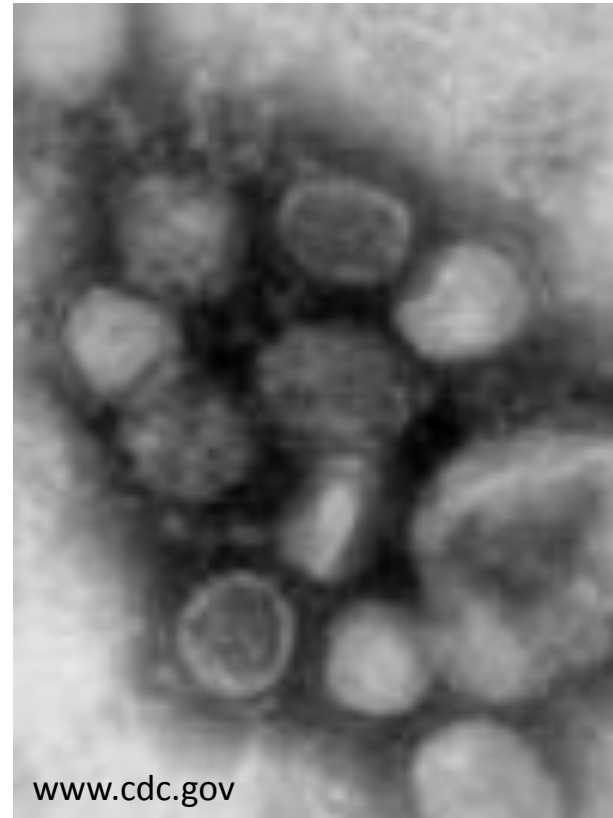


A/California/04/09 VLPs and Influenza Virus Particles

H1N1 VLPs



H1N1 Virus



www.cdc.gov



H1N1 2009 Influenza VLP Vaccine

Mexico Trial



- A/California/04/2009 VLPs
- 5, 15, 45 µg/0.5 mL IM dose
- No adjuvant
- No preservatives
- Stored 2 – 8° C



H1N1 2009 Influenza VLP Vaccine Mexico Study

Stage A

Endpoints:

1. All Adverse Events (AEs) through 3 wks post-dose (PD)2
2. Serious AEs through 6 months PD2
3. HAI assays – Predose 1, 2 wks PD1, 2 wks PD2
4. Exploratory: MN and NAI assays

N=1000
(750 VLP/250 Placebo)

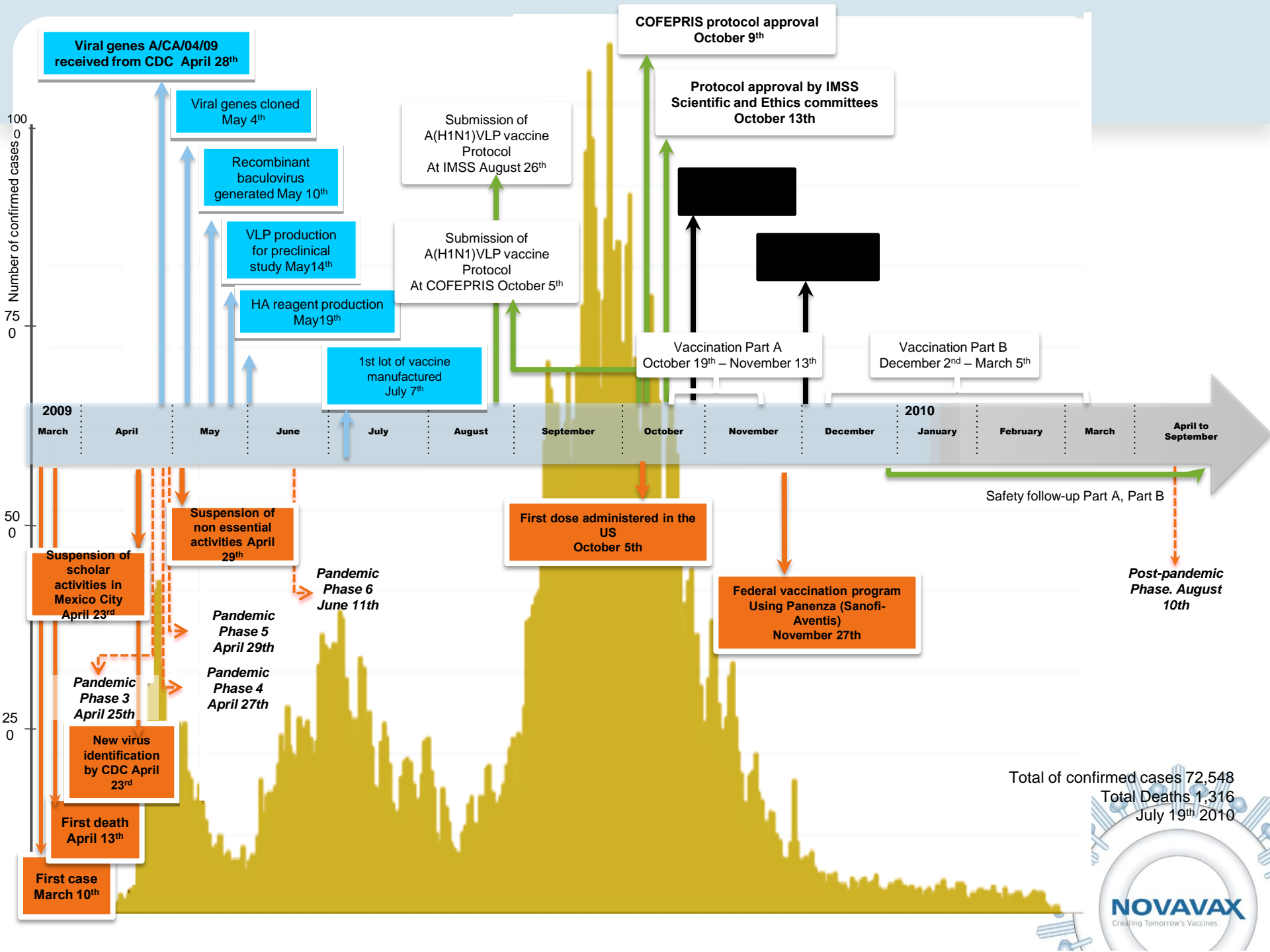
Stage B

Endpoints:

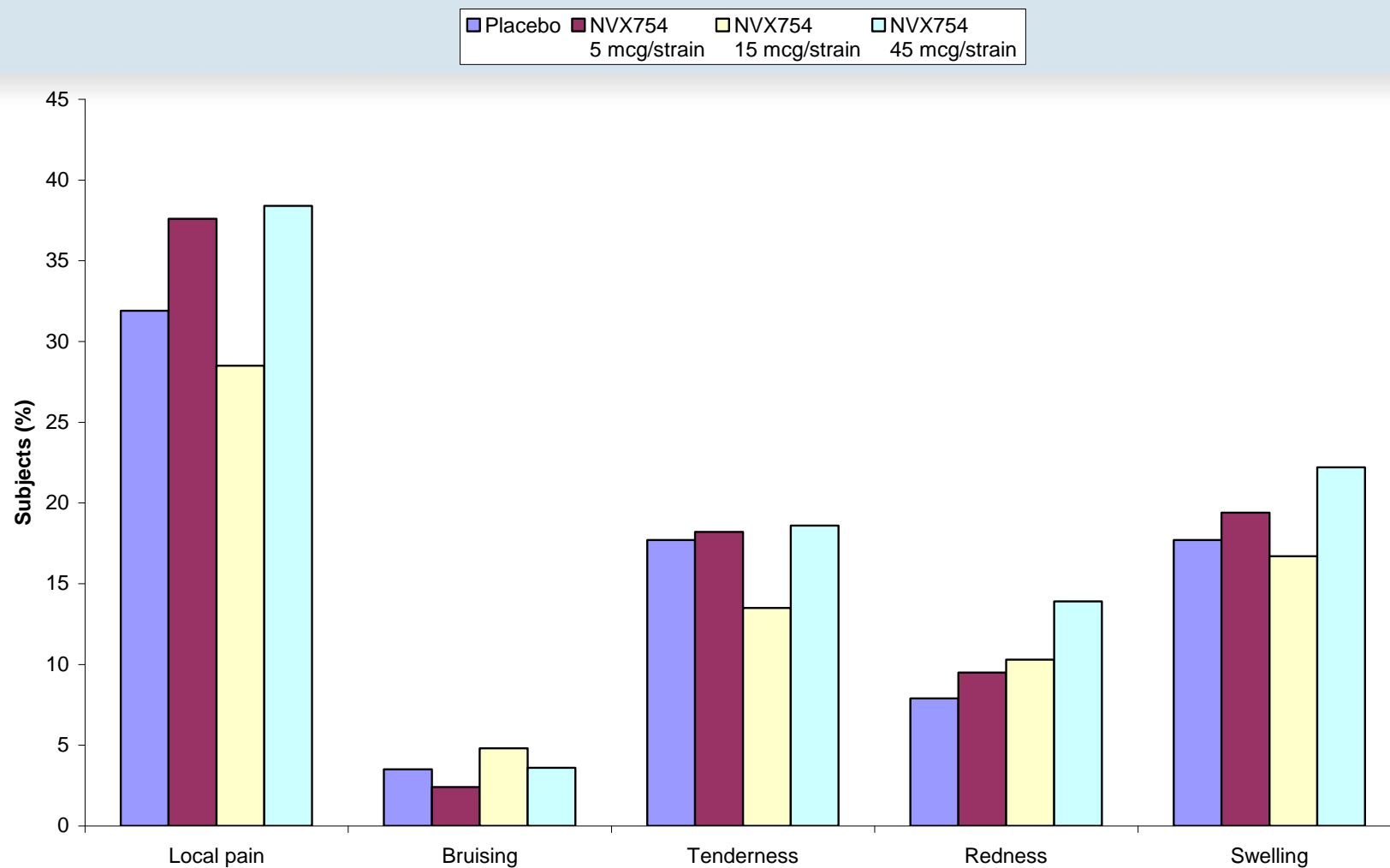
1. Safety, including unsolicited AEs, doctor's office visits, hospitalizations, meds, and SAEs through 6 months PD2

N=3500
(3000 VLP/500 Placebo)

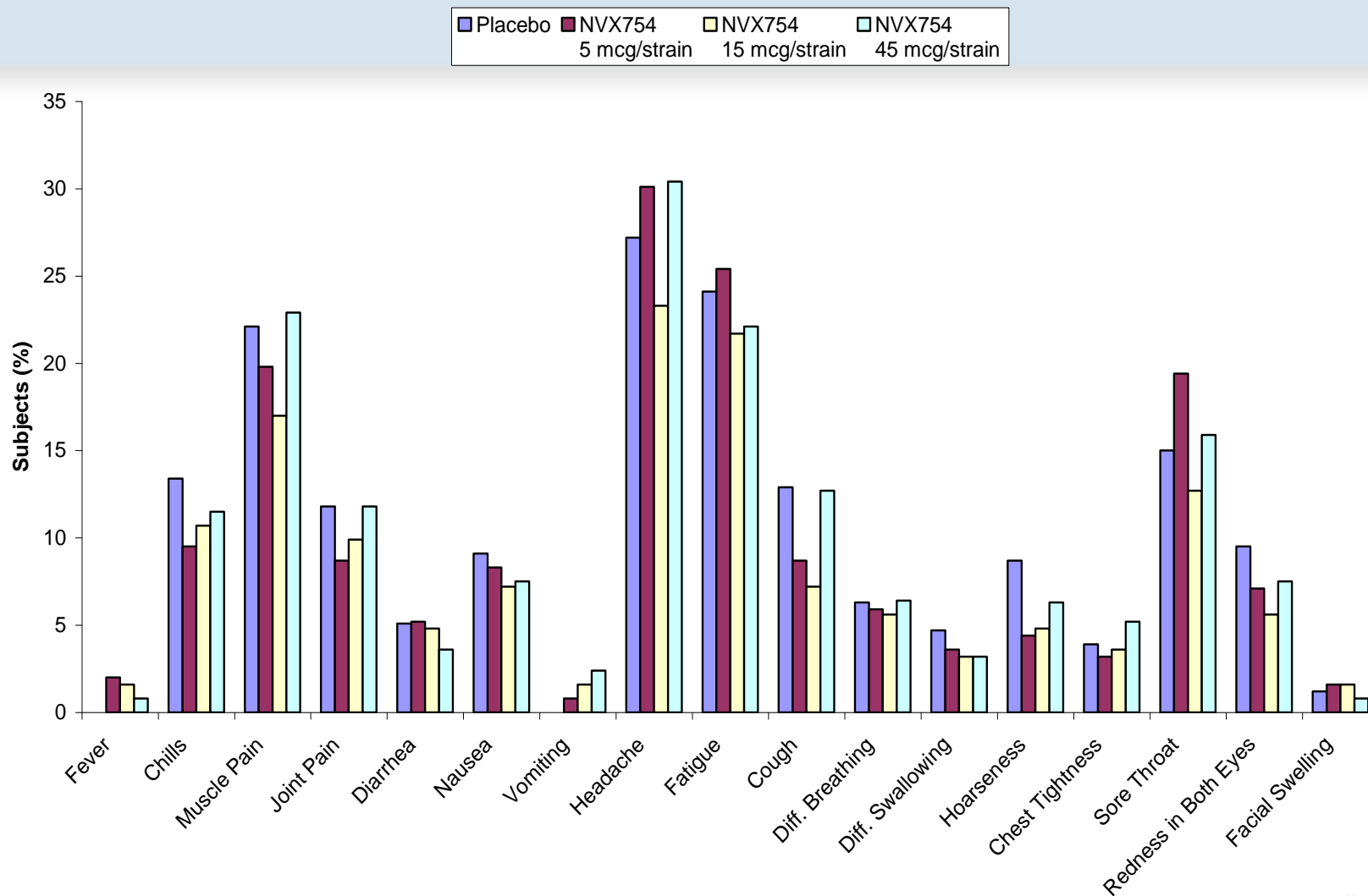




Local Events after First Dose



Systemic Events after First Dose



Final Day 14 HAI Results from Part A

Strain	HAI Parameter	Percent (95% CI) with Response by Vaccination Group (n=963 pp)			
		5 ug n=236	15 µg n=242	45 µg n=243	Placebo n=242
H1N1 A/Cal/04/ 2009	% \geq 4-fold rise	48.5 * (41.9-55.1)	64.7* (58.3-70.8)	75.2* (69.2-80.6)	5.9 (3.3-9.7)
	% \geq 1:40	81.5** (76.0-86.3)	90.5** (86.0-93.9)	91.6** (87.3-94.8)	40.1 (33.8-46.6)
	GMT	87.4 (74.4-102.6)	138.4 (119-161)	173.1 (146.6-204.4)	23.7 (20.1-27.8)
	GMR	4*** (3.4-4.7)	6.6*** (5.6-7.8)	8.7*** (7.3-10.4)	1.2 (1.0-1.3)

* Meets FDA guidelines for seroconversion—lower 95% CI \geq 40%

** Meets FDA guidelines for seroprotection—lower 95% CI \geq 70%

*** Meets EMEA guidelines for GMT Post:Pre ratio \geq 2



Conclusions – Mexico Study

The 2009 H1N1 VLP was well tolerated

- Local and systemic reactogenicity similar to placebo
- No drug-related severe or serious adverse events reported

Immunogenicity responses at Day 14 post dose 1

- Above the lower bound 95% CI for both seroconversion (40%) and seroprotection (70%) at 5, 15 and 45 mcg levels
- 5 mcg dose was safe and immunogenic
- 15 mcg appears to be the optimal dose to provide coverage to broader age range and was selected for further testing in Stage B

Speed of VLP platform technology was demonstrated with production of a cGMP vaccine batch within 11 weeks



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VLP Vaccine Production Plant in Rockville, MD

- 10,000 ft²
- Class C HVAC System
(Class B for Seed Prep)
- Capacity from
1 x 200L and 1 x 1000L (up
to 3 x 1000L)
- Operational at 1000L



Demonstration of

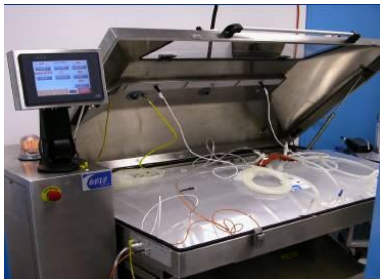


Surge
Economics
Modular prototype

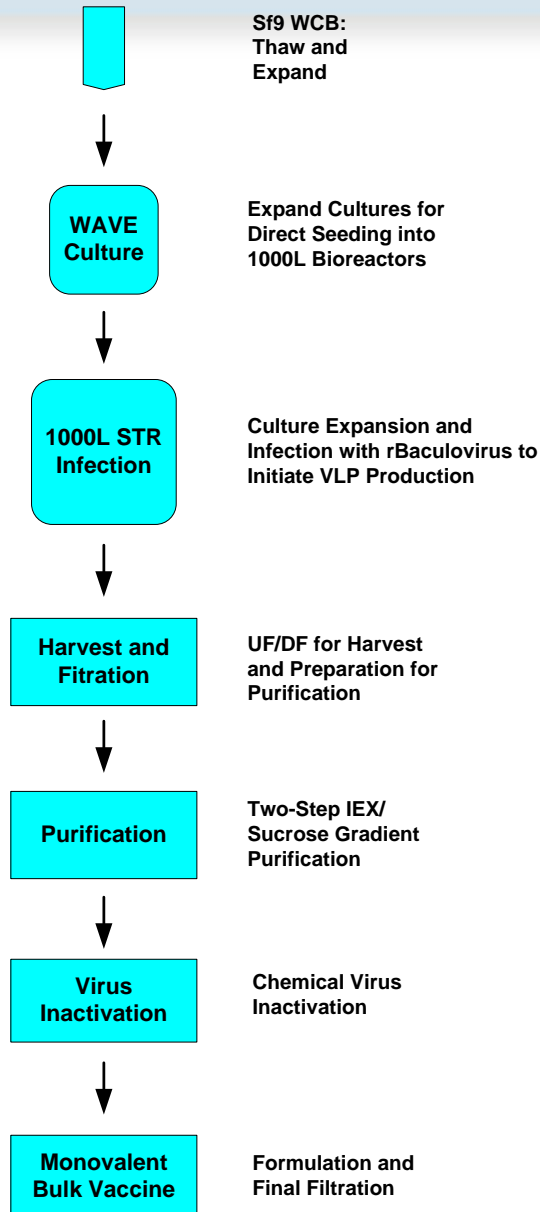


Manufacturing VLPs in Insect Cells

Insect Cell Culture-Based Flu Vaccine Production using a mix of disposable & traditional Systems



Surge Capacity



- Cell culture to bulk vaccine: 3 weeks
- Cycle time at steady state: 9 days
- Productivity achieved: Greater than 1,000,000 doses (15 mcg) per 1000-L reactor

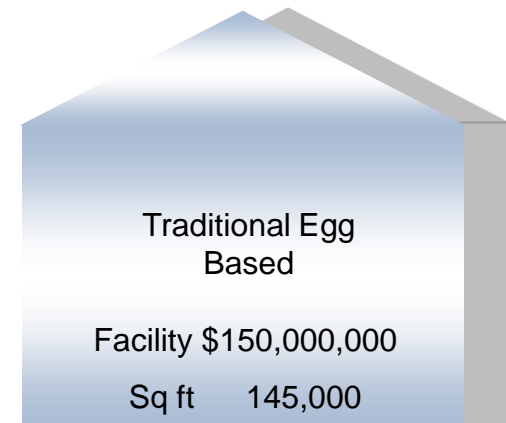


Influenza Vaccine Production Capacity

Modular & Portable Approach

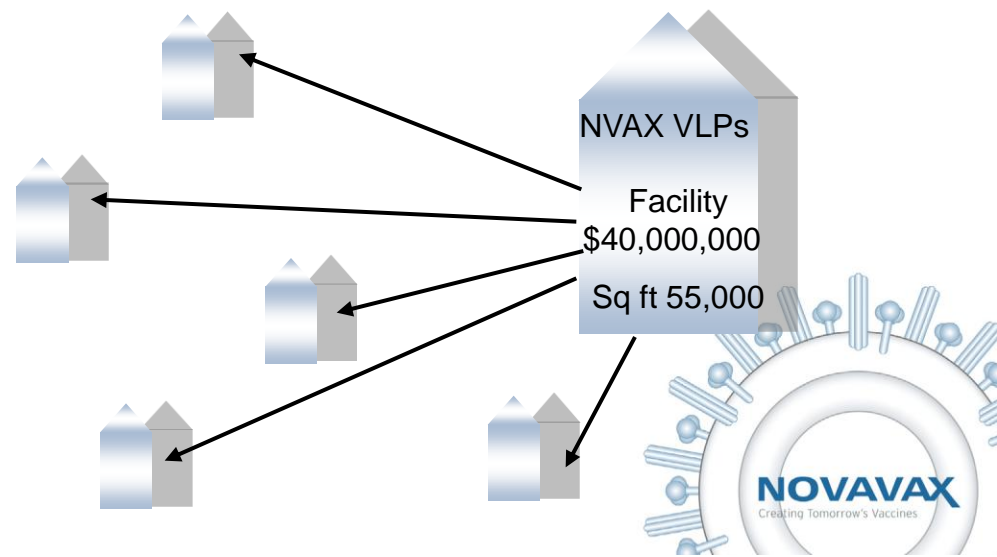
Traditional Flu Vaccine Production:

- Large, central manufacturing facilities
- Supported by complex site infrastructure
- ~100M doses capacity for economy of scale
- Cost: \$150 – \$600M per plant



Insect Cell Culture-Based Flu Vaccine Production:

- Distributed manufacturing
- Facility where vaccine is needed
- Requires little local infrastructure
- 10 – 50 M dose plants
- COGS not dependent of scale
- Cost: 10-20% of traditional facility



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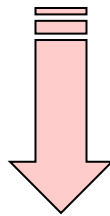
Cadila JV (India)
CPL Biologicals



International Technology Transfer

Success Factors for Tech Transfer

- Less dependence on fixed, integrated equipment & facility
- Portable, reproducible process
- Process and product characterization assays
- Simultaneous process and assay transfer
- Process validation



The CPL Biologicals Case Study

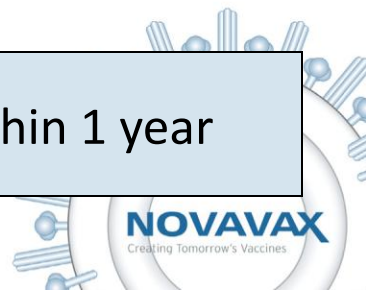


Technology Transfer to India

- Novavax formed Joint Venture with Cadila Pharmaceuticals Ltd (March 31, 2009)
- Influenza VLP Process Technology Transfer Initiated (May, 2009)
- Facility Design Initiated (June, 2009)
- Facility Ground Broken (November, 2009)
- Facility Expected Completion (May, 2010)
- Process, Analytical Transfer Ongoing in Parallel
- Facility Commissioning and Validation (July, 2010)



Implementation of a new functional modular facility ready within 1 year





CPL BIOLOGICALS PVT. LTD.

A Division of Cadila Pharmaceuticals Ltd.
Joint Venture with Novavax Inc. USA

Novel affordable vaccines

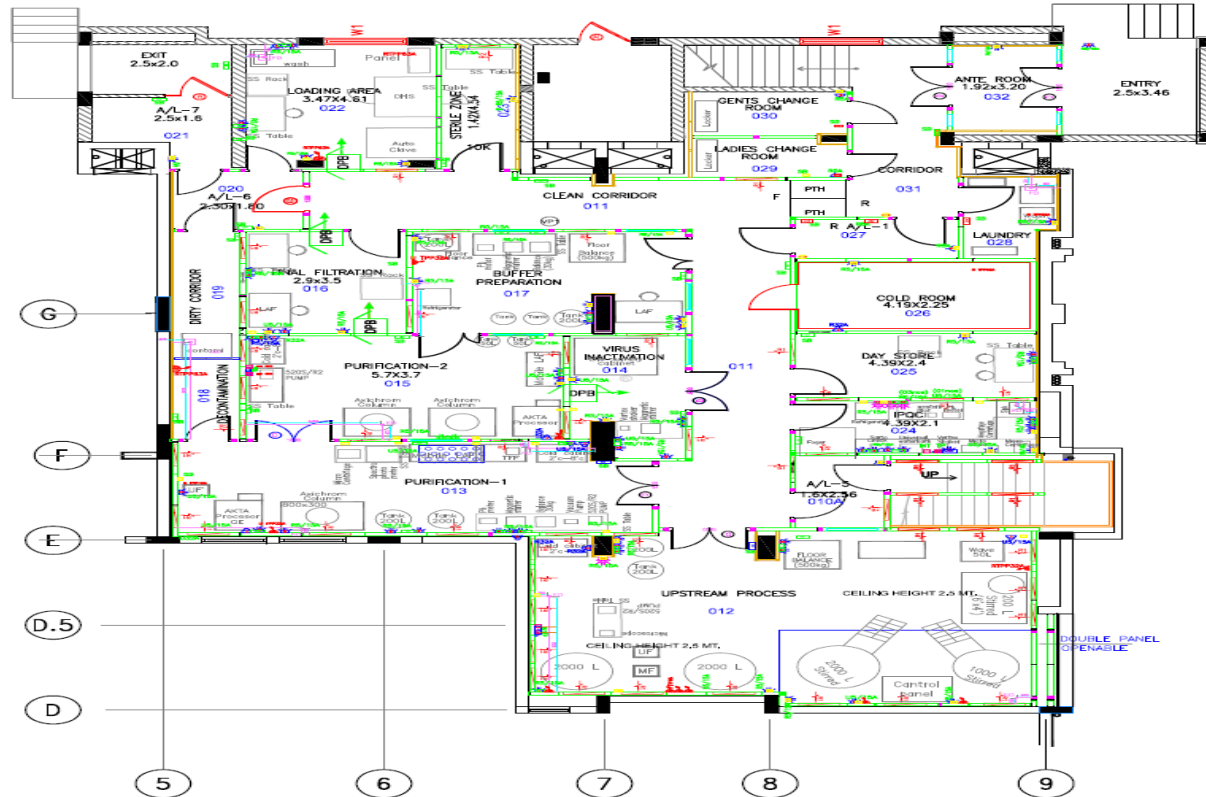
A Division of Cadila Pharmaceuticals Ltd.
Joint Venture with Novavax Inc. USA



Ground Floor Plan

PRODUCED BY AN AUTODESK EDUCATIONAL PRODUCT

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LEGENDS FOR RISER

SL. NO.	SYMBOL	DESCRIPTION	DUCT WIDTH	ROOF CUTOUT (mm x mm)	SPILL OVER (mm)	PERFORATION (mm)
R1		750 x 90 mm RETURN AIR RISER (016 CFM) 650 x 400 mm	750	400x400	407x397	617x627
R2		650 x 90 mm RETURN AIR RISER (076 CFM) 450 x 400 mm	550	400x400	417x397	417x397

ELECTRICAL LEGEND

CODE	SYMBOL	DESCRIPTION	WIRE SIZE	QUANTITY
1		250 WATTS	750/75450	1200
2		1000 WATTS	1000/10000	1200
3		1400 WATTS	1400/14000	1200
4		2100 WATTS	2100/21000	1200
5		2500 WATTS	2500/25000	1200
6		3000 WATTS	3000/30000	1200
7		3500 WATTS	3500/35000	1200
8		4000 WATTS	4000/40000	1200
9		4500 WATTS	4500/45000	1200
10		5000 WATTS	5000/50000	1200
11		5500 WATTS	5500/55000	1200
12		6000 WATTS	6000/60000	1200

R-03	REVISED STAIR CASE AREA (10x0)	22.05.10
R-02	REVISED AS PER CLIENT COMMENTS	08.03.10
R-01	REVISED AS PER APPROVED DRAWING	23.11.09
REVISION	DESCRIPTION	DATE
<div> </div> <div> CADILA PHARMACEUTICALS LIMITED SURVEY PLOT NO.-1389, TRASAD ROAD, DHOLKA </div> <div> RESEARCH & DEVELOPMENT LAB (API) CLEAN ROOM LAYOUT GROUND FLOOR FOR API FACILITY </div> <div> MW HIGH TECH PROJECTS (I) PVT.LTD. </div>		
<div> NAME DATE CHECKED APPROVED </div>	<div> DATE DATE DATE DATE </div>	<div> AS SCALE 1:1000 SHEET 1 OF 1 REV. 02 </div>
<div> PROJECT : CADILA PHARMACEUTICALS LIMITED TITLE : RESEARCH & DEVELOPMENT LAB (API) CLEAN ROOM LAYOUT GROUND FLOOR FOR API FACILITY </div> <div> DATE 08/11/09 BY 08/11/09 FOR 08/11/09 </div>		

Down Stream Set-up



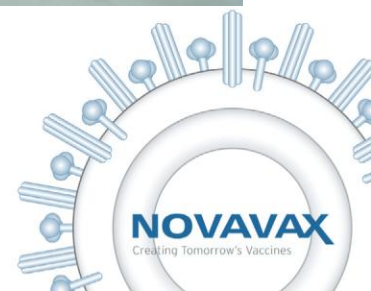
Reactors



Wave Reactor



Purification



Purification Set-up



Virus Culture



Cell Storage





Purification Set-up



Virus Inactivation



Buffer Preparation



Stirred Reactor



Virus Culture



Progress Towards our Quest for a Global Influenza Vaccine Solution

After over \$100MM investment !

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Thank You

Budding Influenza Virus



Virus-Like Particle

